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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/181,027	10/27/98	HAAF T	A-65680-4/RF

HM12/0130

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EXAMINER	
BRUSCA, J	
ART UNIT	**PAPER NUMBER**
1631	13

DATE MAILED: 01/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/181,027	HAAF ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-45 and 47-55* is/are pending in the application.

4a) Of the above claim(s) *45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-44 and 47-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. This application contains claim 45 drawn to an invention nonelected with traverse in Paper No. 6. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 47-55 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention in the Office action mailed 4/25/00 is maintained.

The claims are drawn to human cells comprising two recombinant nucleic acids, one comprising a Rad51 gene, and the second comprising a tumor suppressor gene. The specification does not disclose human cells comprising the two claimed recombinant nucleic acids, nor does it disclose a method of using such cells. The instant specification discloses methods of using the claimed combination of nucleic acids for producing encoded proteins for use in binding assays on page 23 and for generating specific antisera for in situ staining on page 31. The specification discussed on pages 26-27 combinations of Rad51 and tumor suppressor genes for the purpose of

expressing the genes individually so that the expressed proteins may be isolated and purified. The Rad51 and tumor suppressor proteins must be individually purified for use in binding assays and to generate antisera.

4. Applicant's arguments filed 10/30/00 have been fully considered but they are not persuasive. The applicants state that the specification as filed describes the claimed invention of claims 47-55, drawn to human cells comprising recombinant constructs encoding both Rad 51 and a tumor suppressor. Although the applicants have pointed to numerous passages of the specification in support of description of the invention of claims 47-55, inspection of the cited passages fails to reveal any discussion of the cells of claims 47-55. The specification does not describe human cells with the two recited recombinant constructs with such clarity that one of skill in the art would appreciate that the applicants had possession of the cells of claims 47-55 at the time of filing of the instant application.

5. Claims 40-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. It is brought to the applicant's attention that for the purposes of examination the phrase "pharmaceutical composition" is interpreted to mean a composition that can be used to provide a therapeutic benefit to a recipient of the composition.

7. In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of

experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must use the claimed polynucleotide composition encoding Rad 51 and a tumor suppressor protein to produce a therapeutic benefit to a recipient. For the reasons discussed below, there would be an unpredictable amount of experimentation required to use the claimed invention.

b) The specification does not present specific guidance to use the claimed polynucleotide composition encoding Rad 51 and a tumor suppressor protein to produce a therapeutic benefit to a recipient.

c) The specification does not present a working example of using the claimed polynucleotide composition encoding Rad 51 and a tumor suppressor protein to produce a therapeutic benefit to a recipient.

d) The nature of the invention, gene therapy, is complex.

e) Orkin et al. shows that gene therapy has not been successfully practiced in human subjects. Orkin et al. shows in Table 1 that all known vectors for therapeutic nucleic acid delivery have limitations that prevent successful use. The Orkin reference states on page 13 that

"Although widely referred to as 'clinical trials,' gene transfer protocols to date are in truth small scale clinical experiments. Such exploratory studies are meant to test the feasibility and safety of administering particular vectors and to evaluate the effects of expressing specific gene products. Because these studies have not been designed to

measure efficacy, they do not include sufficient controls to evaluate the true merits of gene therapy or compare this approach with conventional approaches to the same disease."

Orkin states on page 5 regarding gene therapy that requires expression of a single gene product:

Although "gene addition" is the simplest strategy for somatic gene therapy, several practical difficulties need to be addressed. Particularly important among these is the need in many instances to deliver the appropriate gene to a specific cell type or tissue. Other challenges include gaining access to the relevant cell type for correction, assessing the total fraction of cells in a tissue that needs to be corrected, achieving the level of expression required for correction, and regulating expression of the added gene once it is transferred into appropriate target cells.

f) The skill of those in the art of gene therapy is high.

g) Orkin et al. shows that there is a great deal of unpredictability in developing effective gene therapy protocols.

h) The claims are broad in that they are drawn to compositions comprising polynucleotides encoding Rad 51 and a tumor suppressor protein that must be used for gene therapy.

The skilled practitioner would first turn to the specification for guidance in using the claimed composition for gene therapy. However, the specification does not provide specific guidance or working examples to use the claimed pharmaceutical compositions for gene therapy. As such, the skilled practitioner would turn to the prior art for such guidance, however Orkin et al. shows that gene therapy has not been successfully practiced in the prior art and that a great deal of unpredictability exists in the use of gene delivery methods in animals. Finally said practitioner would turn to trial and error experimentation to use the claimed compositions to practice gene therapy without guidance from the specification or the prior art. Such represents undue experimentation.

Claim Rejections - 35 USC 102

8. The rejection of claims 40 and 43 under 35 U.S.C. 102(a) as being anticipated by Sharan et al. (Reference 3 in the Form PTO 1449 received 4/15/99) in the Office action mailed 4/25/00 is withdrawn in view of the amendment received 10/30/00.

9. The rejection of claims 40 and 41 under 35 U.S.C. 102(b) as being anticipated by Sturzbecher et al. (Reference 2 in the Form PTO 1449 received 4/15/99) in the Office action mailed 4/25/00 is withdrawn in view of the amendment received 10/30/00..

10. The rejection of claims 40 and 42 under 35 U.S.C. 102(a) as being anticipated by Scully et al. in the Office action mailed 4/25/00 is withdrawn in view of the amendment received 10/30/00.

Claim Rejections - 35 USC 103

11. The rejection of claims 40 and 44 under 35 U.S.C. 103(a) as being unpatentable over Sturzbecher et al. in view of Scully et al. in view of Sharan et al. in the Office action mailed 4/25/00 is withdrawn in view of the amendment received 10/30/00.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca, Ph.D. whose telephone number is (703) 308-4231. The examiner can normally be reached on Monday -Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

John S. Brusca, Ph.D.
Primary Examiner
Art Unit 1631

jsb
January 27, 2001